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Presentation of Case by William I. Coldwell, M.D.

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SOUTHWESTERN MEDICINE

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Scoliosis

Early Diagnosis

By HERBERT E. HIPPS, M.D., *Waco, Texas*

You—the general practitioner, the family doctor, and the pediatrician—you can do more to prevent the severe, grotesque deformities from scoliosis than all the orthopedic surgeons in the world. This is true because you are the ones who see and can diagnose scoliosis in its incipiency.

Scoliosis is very much like many other deformities and many other diseases. If it is caught early, it can be "cured."

The orthopedic surgeon seldom sees scoliosis patients until they are in the nine to sixteen year old age group. At that time, as a rule, a considerable curve with rotation and fixation has developed. **A fixed deformity** is present, which seldom can be completely corrected.

If the orthopedic surgeon could see the child when the scoliosis is extremely mild, when it first begins, then the treatment program would be less hazardous, less expensive, less time-consuming, and the end-result would be immeasurably improved.

Possible to Recognize Early

It is possible to recognize scoliosis early, long before the curve becomes fixed and long before rotation sets in, and you, the family doctor, you are the one who is going to have to find it, simply because in the very early stage of scoliosis, the mother doesn't see anything wrong with the child's back, and you won't either, unless you keep in mind the possibility that such a condition might exist and know how to recognize it.

Look at Figure 1. Anyone can recognize that this seven year old child has scoliosis. Look at Figure 2, which is a standing a.p. x-ray through her spine. She has a severe degree of deformity with rotation of the vertebral bodies and fixation of them in this deformed position.

If this child's curve had been found and treated when she was two or three years old, before it progressed so far, a lot of this deformity could have been prevented.

I shall use this child's photographs to show you what to look for when you examine a child to see if scoliosis is present or not, simply because in this child scoliosis is far advanced and the points to look for are readily discernible.

First of all, have the child stand in front of you with the back exposed with weight equally distributed on both feet, just like the photograph in Fig. 1, (A) was made. Run your finger up and down the spinous processes, thus making a red mark on the skin; this will readily outline the curve for you. Note also that the left scapula is lower than the right one, that the left shoulder is lower than the right. Note that the left loin sinks in more than the right one. Note that the muscles on the right hand side of the shoulder, bridging between the shoulder and neck are more prominent than those on the left. Note also that the left iliac crest seems to be a little higher than the one on the right.

Have the child lean to the left and then to the right. You will notice that the child's thoracic spine bends to the left normally, but it appears to be stiff when she leans to the right. The reason for this is that when she leans to the left, she leans **with** the concavity of the curve. She leans the same way the curve does, but when she leans to the right, she leans **against** the curve and the

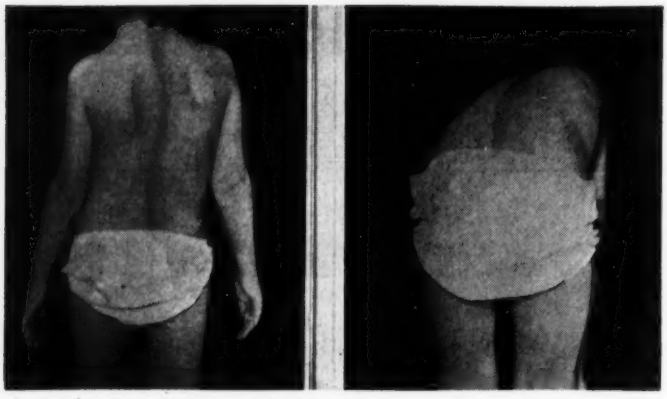

Figure 1

(A) This is an advanced degree of curvature which is easy to see. It is concave to the left in the thoracic spine. Note these associated torso deformities, which are always present with a curvature of the spine: 1. Note that the left loin sinks in more than the right; 2. The left iliac crest appears to be higher than the right one; 3. The shoulder girdle tilts down on the left; 4. One scapula is higher than the other; 5. The muscles between the neck and the shoulder on the right are more prominent than those on the left.

(B) Leaning forward, weight equal on both feet, both knees straight, with her fingers nearly touching the floor. Note the bulging of the thorax on the right, caused by backward bulging angulation of the ribs, which is due to rotation of the vertebral bodies at the apex of the curve.

curve won't straighten, so her thoracic spine appears to be rather stiff.

Now have the child lean forward, and place the fingers of both hands near the floor as in Fig. 1. B. Be sure that she leans straight forward and that both knees are straight. In this patient's case, note the bulging mass on the right hand side in the thoracic area. This is evidence of a fixed rotation in the vertebral bodies.

The vertebral bodies that are in a curve always rotate in such a way that the spinous processes point toward the concavity of the curve. Thus the ribs on the concave side move forward, in front of, or anterior to their normal position, whereas the ribs on the convex side move backward or posterior to their normal position. In this child's case, as you will note, the ribs on the right hand side have moved backward and are forming this hump which you see. The same thing occurs in the lumbar spine when there is a curve there, but in the lumbar area, since no ribs are present, the hump or bulging area is not so large.

When this hump is present on one side of a spine, it practically always means that an advanced degree of curvature is present, that it is a fixed curve, that rotation has occurred, and that a fixed deformity is present.

Now let's look at Bobby M., age 8, Fig. 3. This child was brought to me because of his feet. I did examine his feet, of course, but I also found a very early scoliosis.

Let me show you how in examining this child, I suspected the presence of a scoliosis. You will find in this child almost exactly the same things as noted in the first case, although of a much less degree. Look at Fig. 3 (A). The child is standing naturally, with weight equal on both feet, no elevation under either foot and both knees straight. Notice the asymmetry of the loins, notice that his left shoulder is a little higher than the right, notice that the left scapula is higher than the right and the muscles between the neck and shoulder on the left are a little higher than those on the right. Fig. 3 (B) with the child facing you, note again the asymmetry of the loins. His right side, as you will note, seems to sink in more than the left side. Note the slight tilt of the shoulder girdle.

These things, **if consistently present** while the child is standing, may mean that a scoliosis is present. Certainly the presence of these physical findings should lead you to suspect that one is present.

Figure 2 (C. F.)

This x-ray was made with the child standing naturally, *weight equal on both feet, both knees straight, and no elevation under either shoe. Note the severe thoracic curve with rotation of the vertebral bodies.*

In this child's case, leaning forward revealed no rotational abnormality and right and left bending movements were normal.

Now look at Fig. 4 (A). Here is an x-ray of the child made lying down. As you will note the spine is perfectly straight, but look at Fig. 4 (B). **This x-ray was made with the child standing,** weight equal on both legs, both knees straight and no elevation under either shoe. Now you can see that a slight curve is present. After having seen the standing x-ray, you can understand therefore, why he has the tilted shoulder girdle, and why there is an asymmetry of the torso in the loins.

This child, therefore, has a beginning scoliosis. It is not yet a fixed curve and no rotation is present. Treatment for it at this stage is very simple indeed and the results are uniformly good.

In this particular child's case, I made recommendations in regard to his feet, which is why the child was brought to me, and I also made certain recommendation about treatment of the spine. These were never carried out because the child's father was in military service and they moved away within the next two weeks. It was ten years later before I saw the child again.

During this ten year period of time the child had no treatment for his back. Figure 5 shows you the degree of progression in his curve. It has become greater in degree, rotation has occurred, fixation has occurred, and this eighteen year old child now has a fixed deformity of a considerable degree. This curve can never be completely

(A) The child is standing with weight equal on both feet, knees straight, no elevation under either shoe. Note the asymmetry of the loins, the left scapule is higher than the right and the muscles between the shoulder and neck on the left are higher than those on the right.

(B) Note here that the right loin sinks in more than the left and that the right shoulder is lower than the left.

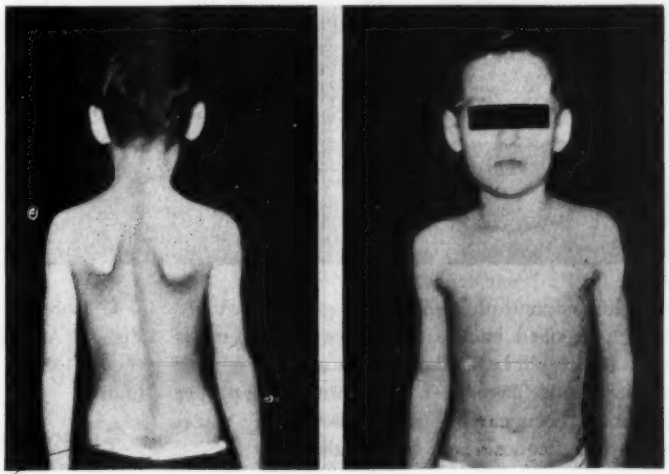

Figure 3 (B. M.)

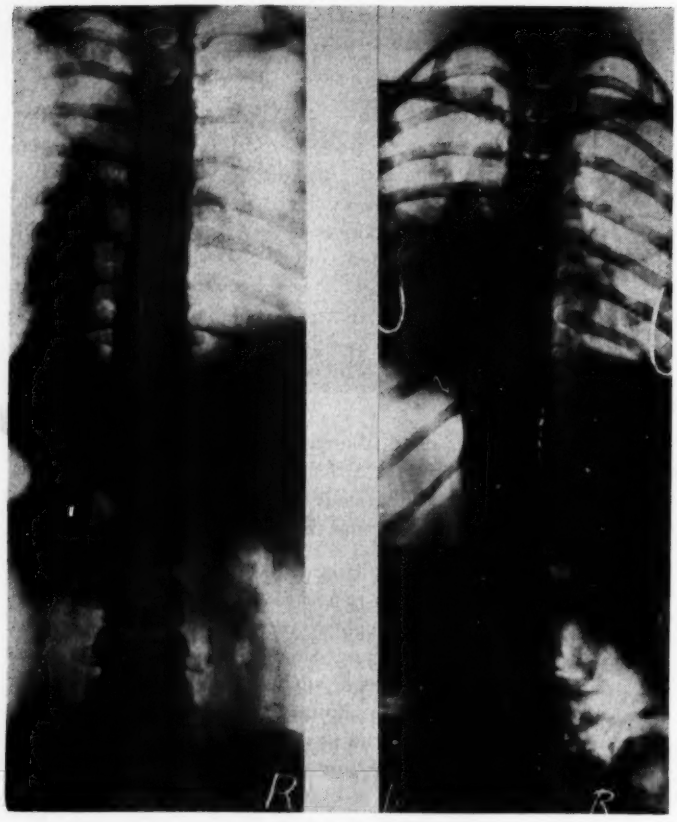

Figure 4 (B. M.)

(A) This film was made with the patient lying supine. The spine is perfectly straight in this supine position.

(B) This film was made with the child standing, weight equal on both feet, knees straight, and no elevation under either shoe. Note the slight curve concave to the right. The left scapula is higher than the right one. This is an early, an incipient curve, not yet fixed, and no rotation is present and it is visible, roentgenologically, only in the standing position.

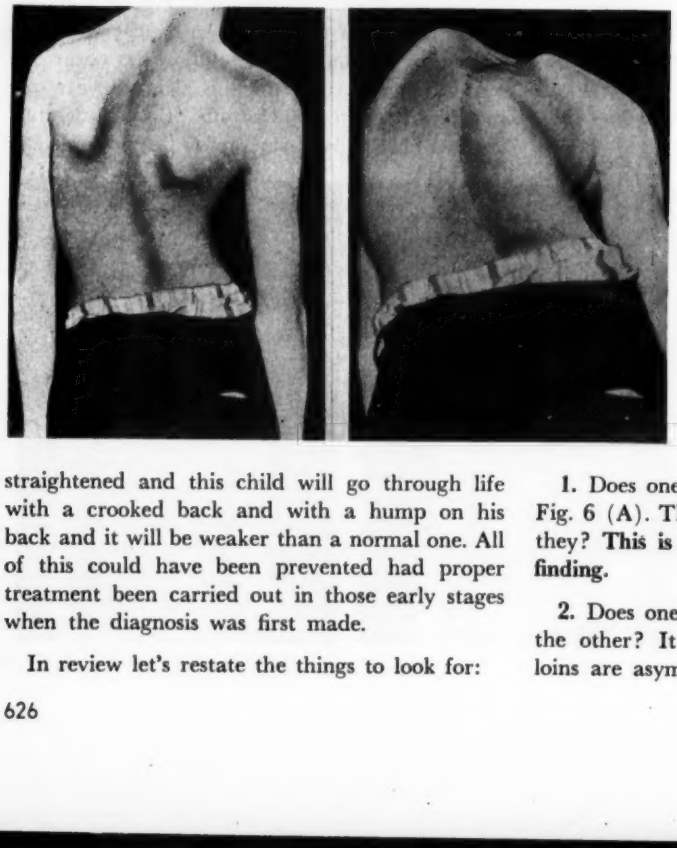

Figure 5 (B. M.)

(A) A marked curve with considerable fixation is now present. Compare this back view with the back view of this same child ten years before, in Figure 3-A.

(B) Note the severe degree of rotation present in this fixed curve, as indicated by the backward bulging rib mass on the left.

straightened and this child will go through life with a crooked back and with a hump on his back and it will be weaker than a normal one. All of this could have been prevented had proper treatment been carried out in those early stages when the diagnosis was first made.

In review let's restate the things to look for:

1. Does one loin sink in more than the other? Fig. 6 (A). The loins should be symmetrical. Are they? **This is the most important early physical finding.**

2. Does one iliac crest seem to be higher than the other? It usually looks this way when the loins are asymmetrical.

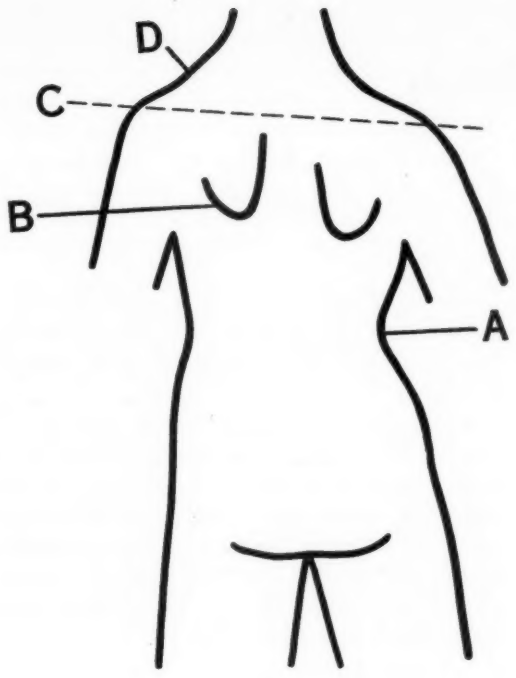

Figure 6

Diagrammatic line-drawing showing specific points to look for in the diagnosis of early scoliosis. As you will note, I have not drawn a line showing the spine curve, because often, very often indeed, in the early curvature you cannot see a curve when you look at the spine alone. The associated torso deformities though, do show up at an early stage, and the things to watch for in the early diagnosis of scoliosis therefore are: D—Prominent muscles between the shoulder and neck on one side. C—Tilted shoulder girdle. B—One scapula higher than the other. A—One loin sinks in more than the other. Also note that the iliac crest appears to be higher than the other because of the way the loin sinks in. The asymmetry of the loins is the most important single physical finding in the diagnosis of early scoliosis.

3. Are the scapulae at the same level or is one lower than the other? Fig. 6 (B).

4. Is the shoulder girdle straight across, parallel to the floor or is it tilted? Fig. 6 (C).

5. Are the muscles between the shoulder and neck more prominent on one side than the other? Fig. 6 (D).

6. Have the child lean forward to see if rotation is present.

7. Have the child lean straight sideways to the left, and then to the right. If motion is free in one direction and not in the other, this might mean a curve is present.

8. **ALWAYS MAKE A STANDING X-RAY.** Have the child stand naturally with weight equally distributed on both feet, no elevation under either foot and with both knees straight.

The two things that are most important of all in the diagnosis of early scoliosis therefore are:

1. The presence of assymetrical loins, Fig. 6 (A).

2. The presence of a curve on a **standing** x-ray.

One scapula being higher than the other might be due to Sprengel's deformity. The presence of thickened muscles bridging across between the shoulder and the neck on one side doesn't always mean a scoliosis. It might be due to a Klippel-Feil Syndrome or to torticollis, but these findings usually mean a scoliosis and if present, certainly should make you suspect that one does exist.

When any of these things is noted, especially the asymmetrical loins, then, by all means, have a standing x-ray made.

You have a double responsibility therefore to your patient insofar as scoliosis is concerned.

1. You must recognize it in its incipiency.

2. You must insist on the family taking the child to an orthopedic surgeon for treatment, because treatment at that early stage is a very simple matter, easy to accomplish, not expensive, and the results are extremely good.

By doing these two things you can save your patient a lifetime of disability.

1612 Columbus St.

Changes Seen in the Eye in Hypertension and Arteriosclerosis

C. H. Fredell, M.D. *Flagstaff, Arizona*

It was Tuerck who first observed the peculiar retinal changes in hypertension in 1850. In 1858 Heymann described the retina in patients ophthalmoscopically and caused considerable controversy.[5]

Wagener has considered the retinal changes and the degree of blood pressure elevation in judging the various types of hypertensive retinal changes as follows:

1. Increased blood pressure which is normal with rest and mild retinal arteriosclerosis.
2. Arteriosclerosis more severe with venous thrombosis and retinitis with permanently elevated blood pressure.
3. Severely elevated blood pressure with angiospasm and retinitis with no papillaedema.
4. Severely elevated blood pressure with angiospastic retinitis with papillaedema.
5. Normal fundus with elevated blood pressure.

The chief value of the Wagener classification is that it enables the physician to determine by means of funduscopic study the degree of progress of the hypertensive disease and its prognostic significance at that time.

The most frequent occurrence of arteriosclerosis is in the late stages of benign hypertension, where arteriolar changes in the kidney seem to be of greatest significance. Sclerosis first affects the vessels in the brain and then the retinal and choroidal vessels, the choroidal more acutely than the retinal.[14]

The first changes we are able to see by opthalmoscopic examination is the loss of the translucency which may be directly attributable to the changes in the vessel wall, particularly the media. There is slight narrowing of the blood column at various points, due to these changes, and thickening of the vessels, but it is not seen diffusely. These vary in caliber while other branches remain, for a long period of time, quite normal in size.[4]

The changes in the vessel walls are seen microscopically as a hyalin degeneration varying from small endothelial deposits to involvement of the entire wall. There is fatty infiltration of the intima or of the entire wall with an ultimate reduplication of the internal elastic lamina and fibrous thickening of the media, with an increased number of fibrils in the adventitia.[6]

The widening of the reflex stripe is due to the change of the reflecting surface from the surface of the arterial blood columns to the outer portion of the arteriole, which was very well described by Gans.[7]

Soon the light reflex is distinct and we are able to see depressions of the vein where it courses below the arteriole. The depression of the vein or "A-V nicking" has been explained by Friendenwald on the basis of having the vein and artery in the same connective tissue sheath at the crossing.[6] All of the layers of the artery are seen to be thickened microscopically, displacing the vein into the deeper layers of the retina.

Reduction in Caliber

The next noticeable change is a reduction in the caliber of the artery with a conspicuous light reflex stripe. There is marked venous compression at its arterial crossing and an enlargement of the proximal portion of the vein and artery. There have been reports of aneurysmal dilatations and irregularities.[1] At this stage many investigators have described the arteries as being "copper wire" in appearance which might be attributed to the thickened opaque media, with a narrowed red column of blood beneath it.

Chief of Surgery, Flagstaff Hospital

The sclerotic changes continue to complete obliteration of the lumen with a "silver wire" appearance of the vessels. The smaller arterioles are involved early. These vessels are ten to fifteen microns in diameter and are found most commonly near the macular and peripheral regions.[7] The vessels are wider than the blood column seen previously, hence a wider more visible light reflex of increased brillance is seen.[5]

In addition to a "silver wire" appearance of the vessels near the macular and distant peripheral regions there is an irregular tortuosity and fine localized variations in the caliber of the arterioles generally.

First Description

In 1916 Foster Moore gave the first good description of the variegated retinal picture due to arteriosclerosis. The vessel changes are essentially the same whether of senile, hypertensive, diabetic, or nephritic origin.[12]

Rarely are only vessel changes seen in an arteriosclerotic patient's fundus, particularly in the younger age groups.[8] The younger age groups are usually diabetic, where the arteriosclerosis is quite severe. The severity of sclerosis is related to the duration of the diabetes and the degree of the metabolic disorder. Changes in the retinal substance are seen in addition to the characteristic vessel changes.

There is a central punctate retinitis which enlarges and coalesces. Hemorrhages and exudates usually precede the white blotches which are evidence of retinal atrophy and scarring.

There is sclera visible in many areas. These hemorrhages and exudates are due to injury to finer arterioles and an altered capillary fragility in that particular region with extravasation of blood into the retinal substance. With more severe injury of the choroidal vessels, chorioretinosis is seen more often than a retinosis alone. With resolution of the hemorrhages there is proliferation of the pigmented epithelium near the atrophy.

The degenerative changes have been thought to be lipid and hyalin deposits. Many investigators[3] believe that the retinal changes are not the result of disturbed metabolism but due to the vessel changes per se.

In addition to the previously mentioned vessel changes, occasionally the retinopathy of nephritis affects the optic disc. In the retina we see hemorrhages, either superficial or deep in location. They usually vary in number, depending on the elevation of the blood pressure and the duration of the disease. They are round, irregularly shaped, linear or flame shaped.

The round and irregular hemorrhages seem to occur at the periphery of the fundus and the linear and flame shaped ones occur more centrally. Some of the hemorrhages are absorbed rapidly and completely while others are converted into white or yellow areas. The latter are sharply delineated and shiny, with little edema near them, while the former have a hazy outline with evidence of edema causing a "cotton-wool" appearance. The multiple small areas of change are the most commonly found.

Histologically one finds most of the hemorrhages in the nerve fiber layer although the more peripheral lesions are deeper. Cholesterol and lipoid disintegration products of the nervous elements form white spots which are more punctate peripherally.

When the hemorrhage is reabsorbed, cyst-like spaces persist and are filled with hyalin colloidal substance which appears yellow and shiny.[6] Absence of retinal tissue over the choroid is also seen.

In the very late stages of arteriosclerosis with retinopathy one finds a stellate shaped group of white spots radiating from the macula. The reason for this configuration is not known and histological studies have been non-contributory.[14]

Loss of Vision

One of the serious complications of arteriosclerosis with hypertension is thrombosis of the central retinal artery. The event is usually heralded by painless, sudden and complete loss of vision in one eye. Ophthalmoscopic examination reveals a marked pallor of the fundus, except for the macular region which is cherry red in color. This is due to the fact that the retina is thinnest at this point so that the red of the underlying choroid is seen.

The nerve is pale, the vein normal or slightly decreased in size and the artery very small with little blood in it. Some signs of retinal edema are seen by the radial reflex lines about the macula. In a certain number of cases a cilio-

retinal artery from the circle of Zinn supplies the macular region. In such cases a small area of central vision is fairly well preserved.

Often the retinal artery occlusion lasts only a few hours as a complete one soon becomes incomplete and a certain amount of function is restored. The color of the retina slowly returns to normal but the disc remains atrophic.

The artery and the vein are in close proximity behind the lamina cribosa. They are included in a common sheath of tissue. Thickening of the arterial wall may be accompanied by a closure of the vein. Closure of the retinal vein also occurs at its "A-V" crossing with sclerotic retinal arteries.

On fundiscopic examination there is seen an intense congestion with enlarged and tortuous veins. Interruptions of the course of the vein at the crossings with the arteries produces a sausage-like segmentation as well as numerous blotchy hemorrhages. Hemorrhages into the vitreous may also occur. The arteries appear to be normal with some edema seen in the central retina. Vision is gradually lost over a longer period of time to a point of blindness. When there is an incomplete closure of the vein the prognosis is good. There is then a gradual remission of the picture.[8]

Transitory Blindness

Transitory blindness has been reported as secondary to arterial spasms of the brain. It may be sudden or gradual in onset and be of a few hours to a few days duration. In conjunction with this vasospastic arteriosclerotic cerebral amaurosis, we always see arteriosclerotic retinopathy.[5]

As the angiospastic changes progress, one can see contractions in most of the retinal arteries and some irregularity in their caliber. This reduction and irregularity becomes more marked with a higher blood pressure prolonged over any period of time. When complete spasm occurs, there are mere threads seen where vessels formerly were seen.[2, 4]

The vessels show little loss of transparency of their walls and the reflex stripe is not exaggerated. In the earlier phases of angiospasm there is seldom any venous compression at the arterial crossings.

An uncommon accompaniment of angiospasm is sclerosis of the vessels although spasm in the sclerotic vessels is a commonly observed phenomenon.[14] When sclerosis does occur there is a much graver prognosis for the patient. The angiospasm is a disease of young adults and arteriosclerosis is a disease of older age.

When sclerosis does occur, the retinal changes are much more numerous when there are angiospastic episodes. The exact onset of sclerosis in retinal vessels is unknown. Changes in the vessels have been observed ten days after the angiospastic onset.[16]

In the severe, "malignant," vessel spasm one sees retinal edema with occasional detachment of the retina, cotton-wool patches, hemorrhages, ganglioform swellings of the nerve fibers, and deposits of hyalin and lipid. There is an occassionally seen star-shaped figure in the macular region, and occasionally papillaedema occurs. Often there is increased intracranial pressure.[10] These changes are most frequently found in hypertension with sclerotic changes of the vessels.

Toxemias of Pregnancy

Acute angiospastic retinitis is commonly seen in glomerulonephritis in toxemias of pregnancy, and in lead poisoning.[5, 13, 15] The picture of acute angiospastic retinitis varies greatly. There are no sclerotic vessel changes. The retinitis per se is due to acute decompensation of the retinal circulation secondary to occlusion due to severe spasm.

The prominent changes in the retina are edema, hemorrhages, exudates and "cotton-wool" patches. If it persists longer than usual, the hyalin and lipid deposits are seen as well as the star-shaped figure in the macular region. Retinal detachment may occur when the edema accumulates in one area.

In most cases, after acute spasm resolves,[29] whether due to termination of the pregnancy, the remission of the nephritis, or the treatment of the lead poisoning, the recovery of the retinal integrity is complete. In the severe malignant hypertensive toxemias of pregnancy, arteriolar necrosis has been reported with residual scarring.[10]

Perhaps one of the most frequently written about phases of the hypertension problem in relation to eye changes is the one of diffuse arteriolar constriction with or without neuroretino-

pathy. It is seen, as is the angiospastic retinopathy, most commonly in the malignant essential hypertension, glomerulonephritis, and hypertensive toxemias of pregnancy. The greatest difference between the two is the involvement of the optic disc or the papilla.

The disc is edematous, reddened and sursounded by retinal swelling. The appearance of the disc is attributable to the contraction of the arterioles with secondary edema and venous hyperemia. In glomerulonephritis the retinal changes usually precede the disc changes.[9] If retinal lesions progress, the papillaedema may improve and atrophy will supervene.[15]

Recession of papillaedema has been observed in few cases of malignant essential hypertension in terminal phases where the cranial pressure was elevated and removal of fluid did not affect the encephalopathy. It was thought that some compensatory mechanism was present in the peripheral vascular supply to the retina where a few normal arterioles absorbed the edema and improved the retinitis.[11]

The retina usually has a gray cloudiness near the papilla due to the edema and ganglioform swellings of the nerve fibers. The gray areas are seen to progress to a white color with evidence of "cotton-wool" patches. The whitish spots progress to bright and shiny or yellowish opague, irregular plaques occasionally surrounded by hemorrhages of varying size.

Several white areas are also seen near large vessels which do not involve the macular region. A "stellate figure" is seen near the fovea. Flame shaped hemorrhages are seen parallel to the vessels and perivascularly. Peripherally they are round and there is a pigment epithelium proligeration.

Pathologically we find a serofibrinous exudate in the papilla and neighboring retina. The spaces between the tissue are filled with fluid and hemorrhages which are seen over the nerve fiber layer. The white spots are large cells laden with fat, lipid and cholesterol esters. Between the retinal elements there is edema with fatty changes of the glial fibers of the nerves and numerous perivascular leukocytes.

The pigmented epithelium has proliferated and the arterioles show hyalinization, fatty changes, necrosis, endothelial proliferation and medial alterations. Acute necrosis of vessel wall results in hyalinization and lipoidosis in precapillary arterioles and even in capillaries or larger vessels.

There is greater obstruction of the vessels in the choroid with lesions of leukocytic infiltration, fibrinous exudation and arteriolar thickening.[6, 16]

We are faced with the necessity of recognizing the malignant phase of "hypertension with neuroretinopathy" since it assumes such great prognostic significance. Subjective optic symptoms of malignant hypertension are color scotomata, especially to blue with high degree of ambliopia, and other symptoms of impaired vision.[5]

The most frequent optic complications of malignant hypertension are the detachment of the retina, closure of the retinal artery or vein, secondary glaucoma, and complete blindness due to encephalopathy.

Summary:

A detailed description of the funduscopic findings one encounters in hypertension and arteriosclerosis has been presented.

It is very important to examine the fundus oculi in all patients suspected of having hypertension and those who have hypertension of any degree. The examination is a very valuable way to follow the progress of the disease and response to therapy. It is hoped this presentation will help the reader obtain a clearer understanding of the changes that are seen, if looked for, in the fundus in hypertension and arteriosclerosis.

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ORTHOPAEDIC MEET HELD AT BEAUMONT — At a meeting of the New Mexico Chapter of the Western Orthopaedic Association held at William Beaumont General Hospital in El Paso September 17 are, left to right, Dr. W. Compere Basom, El Paso, Beaumont consultant; Dr. Jean Cauchoix of Paris, France, guest speaker; Dr. Robert Forbes, Albuquerque, retiring president of the chapter; and Col. John J. Brennan, chief of Beaumont's Orthopedic Service, new president of the chapter. (Official U. S. Army photograph.)

French Surgeon Speaks

To New Mexico Orthopaedists

Dr. Jean Cauchoix, assistant professor of orthopaedic surgery at the University of Paris and author of several books and articles in the orthopaedic field, was the principal speaker at a meeting of the New Mexico Chapter of the Western Orthopaedic Association September 17 at William Beaumont General Hospital.

Dr. Cauchoix discussed fractures and non-unions and reported on cases of non-unions in which iliac bone grafts were combined with firm fixation.

Captain T. B. Horan, M.C., presented a paper on "Surgical Treatment of Malignant Skeletal Tumors". A 25 per cent overall survival rate was reported. Early diagnosis and biopsy were recommended. Amputation provided the best chance for survival, Captain Horan said.

Captain Manfred E. Krause, M.C., spoke on "Congenital Chronic Dislocating Radii of Elbows", a rare condition of which only 36 cases have been reported in medical literature. Captain Horan, in his talk on "Traumatic Dislocation of the Hip", urged that seat belts be worn to prevent such injuries, which are caused by knees striking the dashboard with femurs being driven out through the back of the hip, posterior aspect of the acetabulum.

Captain Krause, in his paper on "Experiences with Chemical Stimulation of Fracture Healing", reported that anti-tuberculosis medications appear to aid fracture healing, according to a preliminary research report at William Beaumont General Hospital.

Clinical Observations on Iron Metabolism in Pregnancy

By Celso C. Stapp, M.D., *El Paso*

Although the development of anemia during pregnancy may be due to several causes, the great majority of those related directly to the pregnancy itself are of the iron-deficiency type.

Because the female with normal blood values is better prepared to withstand hemorrhage at delivery or other obstetric complications and because she is better prepared to provide normal quantities of iron to the fetus, the maintenance of proper blood values during pregnancy has long been of medical interest.

Our concepts of iron metabolism during pregnancy have, however, undergone a great deal of change since the development of newer and better methods of study. It is now recognized that the maintenance and building of reserve storage iron during pregnancy is at least as important as the mere maintenance of the hemoglobin level. Furthermore, the old idea that levels of 10 gms./100 cc. of hemoglobin represent only a "normal" blood dilution during the last trimester of pregnancy is no longer tenable.

Iron-Deficient State

Instead, it seems well established that the fall in serum iron and the increase in erythrocyte protoporphyrin values in pregnant women whose hemoglobin levels fall below 12 gms./100 cc. certainly indicate an iron-deficient state.

New concepts, therefore, place much more emphasis upon the desirability of maintaining and improving the pregnant female's hemoglobin status throughout pregnancy rather than to begin the administration of therapeutic iron when hemoglobin levels have fallen to an arbitrary subnormal point.

Recognition of the fact that the average female is in a precarious state of iron balance and seldom has any significant amount of reserve iron regardless of her hemoglobin level,[1] places even greater importance upon assuring sufficient iron income throughout pregnancy to supply the demand of the developing fetus. Only in this way can hemoglobin levels be maintained, reserve storage iron be protected and the appearance of anemia avoided.

Iron Metabolism in Pregnancy

If we assume that the average woman has 12 gms./100 cc. of hemoglobin and a blood volume of 4,000 cc. at beginning pregnancy, her total hemoglobin mass is 480 gms. This represents about 1,600 mg. of elemental iron. Since she probably possesses little or no reserve storage iron, it is necessary that she supply the needs of the fetus entirely through increased dietary absorption and by the iron conserved through cessation of menstruation.

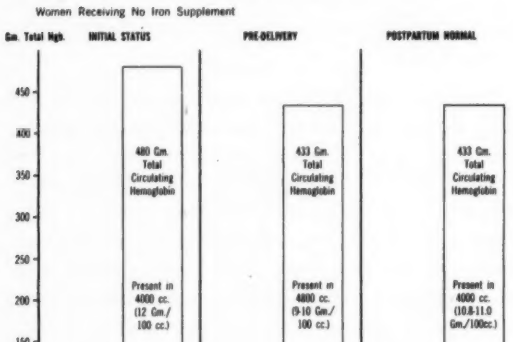
The fetus requires 440 mg. or more of elemental iron. Assuming a normal excretion of one mg. of iron per day, even though the normal rate of absorption doubles to two mg. per day, the diet would add only 280 mg. of iron during the 280-day pregnancy. As a result, 160 mg. of iron would be removed from the blood through the destruction of hemoglobin and eventually appear in the fetus as fetal hemoglobin iron.

This 160 mg. of iron represents the destruction of about 47 gms. of hemoglobin, leaving the woman with a net total of 433 gms. in her normal

blood volume of 4,000 cc. (10.8 gms./100 cc.). This, therefore, would approximate the eventual postpartum hemoglobin level. In the last trimester, when blood dilution may approximate 20 per cent, the same total hemoglobin would be present in about 4,800 cc. of blood to give an apparent value of about nine gms./100 cc. These changes are illustrated in Figure 1 and would occur to a greater or less extent depending upon the actual iron storage reserve present at beginning pregnancy.

Figure 1

Effect of Pregnancy on Hemoglobin and Storage Reserve Iron
(NO THERAPEUTIC IRON SUPPLEMENT)



The body does not put iron into the storage depots until the need for circulating hemoglobin is satisfied. Normal hemoglobin values, therefore, do not in themselves guarantee the existence of any iron reserve. On the other hand, low values almost certainly suggest the practical absence of reserve storage iron.

In other words, the female is likely to show a decrease in hemoglobin during pregnancy regardless of the initial level. The extent and the time of appearance of this fall are dependent upon the time of disappearance of whatever iron reserve is present at the beginning of pregnancy.

Practical Aspects

The above theoretical concepts are subject, of course, to individual variation. That most women, however, do not have sufficient reserve storage iron to supply the demand of the fetus is evidenced by the fact that 80 per cent of pregnant women fail to maintain their hemoglobin during pregnancy. In fact, evidence of iron deficiency appears in most cases when the hemoglobin levels fall below 12 gms./100 cc.[2]

The response to the administration of therapeutic iron during pregnancy is additional evidence for the presence of the iron-deficiency state since, in these circumstances, four of five pregnant women do maintain or improve their hemoglobin.[2]

It is obvious that provision of adequate therapeutic iron to permit the patient to complete the pregnancy without loss of hemoglobin must be a primary therapeutic consideration. Furthermore, even though the patient would have been capable of completing her pregnancy without suffering hemoglobin decreases, the iron deficit due to pregnancy is certain to leave her less well prepared, in terms of iron reserve, for subsequent menstrual blood loss or subsequent pregnancies.

Therapeutic

For these reasons it is entirely rational to administer therapeutic iron to all pregnant patients. Such a practice can, in most instances, prevent a precipitous fall in hemoglobin levels and the development of a severe anemia even in women with little or no reserve storage iron. It may also provide a postpartum iron reserve as protection against subsequent iron deficiency.

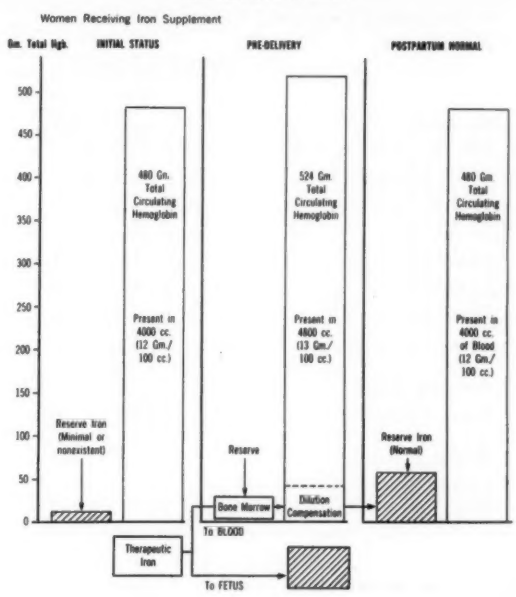
The value of routine therapeutic iron during pregnancy is illustrated in Figure 2. Therapeutic iron serves both to supply the demand of the fetus and to provide new iron for bone marrow synthesis of the hemoglobin needed to compensate for blood dilution. As a result, total circulating hemoglobin is temporarily increased up to the time of delivery. Shortly thereafter, circulating blood values return to normal and the excess circulating hemoglobin is converted to reserve storage iron. Thus, the postpartum woman is in a normal iron status.

Patient's Iron Status

It is obvious that blood values obtained approximately six to eight weeks postpartum will give evidence of the patient's iron status. Other factors

Figure II

Effect of Pregnancy on Hemoglobin and Storage Reserve Iron
(THERAPEUTIC IRON SUPPLEMENT)



being equal, a postpartum hemoglobin level below the initial finding would indicate a continuing chronic iron deficiency state without sufficient iron to permit normal circulating hemoglobin and a virtual absence of reserve iron. On the other hand, postpartum values above the initial values would suggest that the patient had entered pregnancy in an iron-deficient state and had absorbed and utilized additional iron during her pregnancy.

In either case, postpartum iron administration should certainly seem rational. The only assurance that reserve iron existed after completion of the pregnancy would be a series of findings in which pre-delivery values were above those initially found and postpartum values had returned to the initial levels since. This would indicate, of course, that the increased circulating hemoglobin of the last trimester had been returned to storage reserve.

Accordingly, it has been our practice to prescribe a hematinic to all pregnant women beginning either in the first or early second trimester of pregnancy. In addition, we recommend the continued administration of iron for several months postpartum.

Administration of Iron

In our experience, the various inorganic iron compounds appear to be equally efficacious when administered orally. There is certainly little merit to the "shotgun" preparations and this is particularly true of the administration of iron with vitamin B_{12} or other hematinic adjuncts in preventing the ordinary hypochromic anemia of pregnancy. A great many thorough studies have demonstrated that the absorption and utilization of ferrous iron depends primarily upon physiologic factors and not upon the form in which it is administered.

However, the discovery of erythropoietin, the erythropoietic hormone, and identification of its role as the regulator of erythropoiesis[3] may require modification of this concept. The fact that cobalt enhances the formation of erythropoietin in the body led us to evaluate the effect of an iron-cobalt product* as a hematinic agent in pregnant women. Such preparations have previously been evaluated in pregnancy with excellent results in dosage levels providing 600 to 800 mg. of ferrous sulfate per day.[4] In the present study, however, the cobalt was given with only 300 mg. of the iron salt daily. If the increased marrow iron utilization, due to cobalt-enhanced erythropoietin, in turn increased gastro-intestinal absorption as might be expected, then these smaller quantities of iron should prove fully effective. A resulting advantage should be a decrease in the gastro-intestinal intolerance frequently present with the customary required iron dosage. This may be a much more important factor than is often realized since in careful studies intolerance to customary doses of ferrous sulfate has been reported to be as high as 50% of all patients.

Materials and Methods

We have given the cobalt-iron mixture to well over 1,000 pregnant women during the past three years with what we believe to be excellent results. Lack of time prevents preparation and correlation of the resulting mass of statistics but we felt it would be of interest to present data compiled from a series of 40 consecutive cases representative of the over-all group. These are not selected

*The preparation used in this evaluation was Roncovite-MF, Lloyd Brothers, Inc., Cincinnati, Ohio.

cases. They are simply a series of patients seen in the course of practice and should be typical of those seen in the average obstetrical practice in this area.

Fifteen of the group were given the cobalt-iron preparation beginning in their first trimester of pregnancy; 21 began this treatment during the second trimester; four received it only in the three months prior to delivery. The series represented 14 primigravidas. There had been 15 prior recorded abortions or miscarriages divided among nine patients of the group. The dosage prescribed was one tablet three times a day representing 45 mg. of cobalt chloride and 300 mg. of ferrous sulfate.

Hemoglobin Values

Hemoglobin values were determined spectrophotometrically and erythrocyte counts by standard methods by a commercial laboratory except that the first postpartum results were obtained in the hospital laboratory. None of the patients in this series showed evidence of a megaloblastic anemia and, based on the hemoglobin and red cell counts, all were either normochromic or hypochromic. These data represent, of course, the usual accuracy to be expected in daily practice.

Hemoglobin values and erythrocyte counts were done at the time of the initial visit and were repeated two or three times during the pregnancy. Because these values fluctuate widely and are invalid[2] during the last two weeks of pregnancy, we attempted to obtain pre-delivery blood data near to but prior to this time. The average "pre-delivery" data in this series of patients was obtained 6.1 weeks before delivery. First postpartum values were determined on the third postpartum day and "final postpartum values" were determined when the patient was discharged, at the last office visit, usually four to six weeks later.

Results

The average erythrocyte count, the average hemoglobin level and the distribution of individual hemoglobin values for the 15 patients who received the iron-cobalt preparation beginning with the first trimester of pregnancy are shown in Table I. Fourteen of these 15 women maintained or improved their hemoglobin status during pregnancy. Ten of the 15 showed pre-delivery values of 13 gms./100 cc. or better. On the final postpartum count, no patient had less than 12 gms./100 cc. hemoglobin and 14 of the 15 in this series showed values of 13 gms./100 cc. or more.

Table I.

Blood Values of Patients Beginning Treatment in First Trimester

Hemoglobin Gms./100 cc.	No. of Patients at Each Level: Initial Hgb	Pre-delivery Hgb	First Post-partum Hgb	Final Post-partum Hgb
9.0- 9.9	1			
10.0-10.9	3			
11.0-11.9	6	2	2	
12.0-12.9	5	3	1	1
13.0-13.9		4	5	8
14.0-14.9		6	6	6
15.0-15.9			1	
Average Hgb Gms./100 cc.	11.2	13.2	13.4	13.6
Average RBC Count in Millions	3.6	4.0		4.2

Similar data for the 21 patients who received the iron-cobalt preparation beginning early in the second trimester appear in Table II. In this group,

Table II.

Blood Values of Patients Beginning Treatment in Second Trimester*

Hemoglobin Gms./100 cc.	No. of Patients at Each Level: Initial Hgb	Pre-delivery Hgb	First Post-partum Hgb	Final Post-partum Hgb**
9.0- 9.9		1		
10.0-10.9	4	1		
11.0-11.9	8		1	
12.0-12.9	4	3	2	2
13.0-13.9	2	9	9	7
14.0-14.9	2	6	7	7
15.0-15.9	1	1	2	4
Average Hgb Gms./100 cc.	11.6	13.2	13.5	13.9
Average RBC Count in Millions	3.6	3.8		4.2

*Average was fourth month of pregnancy.
**One patient did not appear for final hemoglobin determination.

19 maintained or improved their hemoglobin and 16 of the 21 gave pre-delivery values of 13 gms./100 cc. or more. On the final postpartum count, none were below 12 gms./100 cc. and 18 of the 21 were at the 13 gms./100 cc. level or above.

The four patients in whom treatment was not begun until the seventh or eighth month of pregnancy had an average initial hemoglobin of 11.5 gms., an average pre-delivery value of 13.4 gms. and an average final count of 13.3 gms. All four of these had maintained their hemoglobin throughout the second trimester without iron therapy. Shortly thereafter, however, one of these four patients showed a hemoglobin value of only 10 gms./100 cc.

Discussion

In our opinion, the maintenance of optimal hemoglobin levels during pregnancy is an important objective. As Eastman[8] says, ". . . Even the milder anemias are not without their clinical import, for they constitute the most common cause of malaise, weakness, easy fatigability, susceptibility to infection, shortness of breath, and tachycardia." Moreover, anemic patients often have more prolonged labors[9] and infants born of anemic mothers are frequently deficient in stores of iron.[10]

On the basis of accepted standards of 12 to 12½ gms./100 cc. hemoglobin and 4 to 4½ million red cells/cu. mm.,[5] our series of patients was "borderline" anemic at the time of first visit. Despite fetal demand for iron and the "dilution factor" involved in pregnancy, these women improved their hemoglobin and their red cell status quite strikingly during pregnancy. There did not appear to be any significant difference in the response whether therapy was begun in the first or early in the second trimester except that a relatively greater proportion of the group receiving early therapy delivered at levels above 13 gms.

Final Postpartum Values

It is of considerable interest to note that the final postpartum values show only a slight difference from the pre-delivery determinations and are definitely higher than the initial values. These findings certainly suggest that these women had reached their true "normal" at about 13.5 gms./100 cc. of hemoglobin, that they had done so through improved iron utilization despite the abnormal iron demand of pregnancy and that they had initially been much more anemic than previously accepted standards would indicate. Certainly they are better prepared to withstand future menstrual iron deficit and subsequent pregnancy than at the beginning of this treatment. The distribution of patients in Tables I and II shows clearly the effectiveness of therapy in improving the hemoglobin status of these patients.

Four patients who received no iron supplementation during the first two trimesters, completed their pregnancy with satisfactory blood values. This, however, should not be taken to mean that early supplementation is unnecessary since, of the group in whom therapy was not begun during the first trimester, several began to show a fall in hemoglobin values before medication was initiated. In three, the drop was severe (from the 14 to 15 gm. level down to approximately 10 gms./100 cc.).

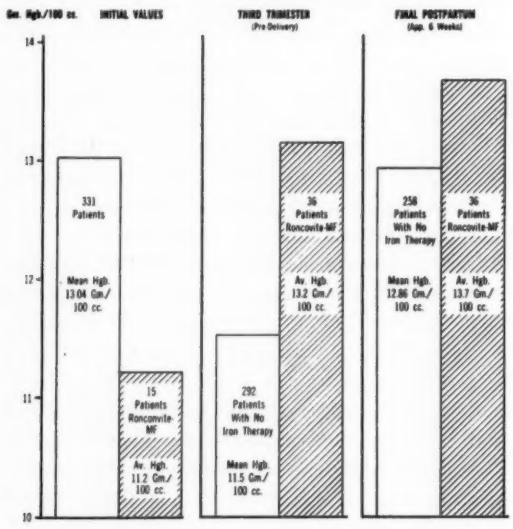
Effect of Pregnancy

The effect of pregnancy on blood values has been thoroughly studied with and without iron supplementation. It is generally accepted that some 80 per cent of pregnant women fail to maintain their hemoglobin during pregnancy unless iron supplementation is given and that even with adequate doses of plain iron compound, one in five pregnant women still fail to maintain their hemoglobin levels[2,4]. In our series, 37 of 40 patients (92½ per cent) maintained or improved their blood status with the administration of the cobalt-iron preparation.

It is also interesting to compare our results with those of Darby, et al.[2] in their comprehensive studies of some 300 pregnant patients receiving no iron supplementation. In their series, mean hemoglobin and red cell values fell throughout pregnancy and final postpartum findings (six weeks or later) were slightly below the initial values. In our group, in contrast, mean values for these indices rose throughout pregnancy and the final postpartum findings were well above initial levels. Figure III shows a comparison of results obtained in the Darby study with those of the iron-cobalt preparation used in our evaluation.

Figure III

Comparison of Hemoglobin Values


Patients Receiving Cobalt-Iron Therapy and those Receiving No Iron Supplement
Gm. Hgb./100 cc.
INITIAL VALUES
THIRD TRIMESTER (Pre Delivery)
FINAL POSTPARTUM (App. 6 Weeks)
14
13
12
11
10
331 Patients
Mean Hgb. 13.04 Gm./ 100 cc.
15 Patients Roncovite-MF
Av. Hgb. 11.2 Gm./ 100 cc.
292 Patients With No Iron Therapy
Mean Hgb. 11.5 Gm./ 100 cc.
36 Patients Roncovite-MF
Av. Hgb. 13.2 Gm./ 100 cc.
258 Patients With No Iron Therapy
Mean Hgb. 12.86 Gm./ 100 cc.
36 Patients Roncovite-MF
Av. Hgb. 13.7 Gm./ 100 cc.

We would interpret this to mean that the "dilution factor" accounted for the decreased hemoglobin levels in the Darby study and that their postpartum findings showed simply a return to the pre-pregnancy "status quo." Our own findings would indicate an acceleration of iron utilization and hemoglobin synthesis with the patient's hemopoietic system more than compensating for the dilution factor so that the postpartum patient is in a better iron status than prior to her pregnancy. Clearly she must have absorbed and utilized more iron as a result of cobalt-iron therapy.

Toxicity and Side Effects

The allergic skin rash exhibited by some patients to cobalt administration, even in the form of vitamin B_{12}, has been reported by Sidell, et al.[7] Two of our patients exhibited a skin rash while under treatment with cobalt-iron. In one patient with a long history of allergy the rash was relieved with pyribenzamine; in the other, therapy was discontinued about one month prior to delivery after seven months' medication.

Constipation was reported by two patients. It is difficult, of course, to ascribe this to our hematinic therapy since it is a common occurrence during pregnancy. There were no other side effects or toxic symptoms which could conceivably ascribe to the cobalt-iron preparation.

Summary

In a series of 40 consecutive pregnant women seen in an obstetrical practice, the use of a cobalt-iron preparation was highly effective in maintaining and increasing hemoglobin values during pregnancy.

Both hemoglobin and red cell values increased despite the dilution factor and fetal iron demand.

Pre-delivery values were as high as final postpartum values, thus indicating that these patients were hemopoietically normal at the time of delivery.

Final postpartum determinations were above those found initially. This suggests that these women had on the average, not only been in a negative state of iron balance at the beginning of pregnancy but were "borderline" anemic.

The reduced iron dosage used in this evaluation appears to obviate many of the side effects usually seen with iron therapy[11] without loss of effectiveness.

The iron-cobalt preparation used in this study appears to be an effective hematinic for routine use in the pregnant woman, and it would appear that the enhancement of erythropoietin production by cobalt improves iron utilization in pregnancy.

604 University Towers

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Clinical Pathological Conference

R. E. Thomason General Hospital, El Paso

F. P. Bornstein, M.D., *Editor,* Case No. 1436, July 21, 1960
Presentation of case by William I. Coldwell, M.D.

History: Dr. Nathan Kleban:

A 65 year old unemployed, married Anglo-American man was brought to the hospital by ambulance at 4:17 a.m. on April 13, 1960.

For two years intermittent epigastric pain had been relieved by milk, Aspirin, Bufferin, or Alka-Seltzer. Appetite was variable. The patient felt weak, tired, and had lost an unknown amount of weight.

Five days before admission the same pain recurred, was severe and accompanied by vomiting of yellow material. The pain persisted with diminished intensity. The patient was brought to the hospital when he vomited an unmeasured amount of blood.

There had been moderate intake of alcohol until two years before admission. There had been no other symptoms or illness.

Physical Examination:

B.P. 70/40; T. 96.8; P. 84; R. 16.

The patient was drowsy, conscious, cold, pale. There was dry blood around the mouth. The lungs were clear. There were no abnormal heart findings. The abdomen was soft, non-tender. The liver was not enlarged.

Hospital Course:

The first unit of whole blood was started, 98 minutes after arrival in the emergency room. On the day of admission a surgical consultant found hypotension, pallor, slight epigastric tenderness, a tarry stool in the rectum. On the same day a medical consultant found no heart abnormality, no liver enlargement and no abdominal tenderness.

Six units of whole blood were transfused. Propantheline bromide (Probanthine), intravenous conjugated estrogens (Premarin), adrenochrome mono-semicarbazone sodium salicylate complex (Adrenosem) and morphine were administered. A soft diet was ordered.

Oxygen by mask for labored breathing was started on the afternoon of the second day. This complaint increased after another unit of blood and one liter of electrolyte solution were given intravenously. The patient was then given intravenous digitalis, aminophyline, and mercurial diuretic. Along with treatment for acute pulmonary edema, levarterenol bitartrate (Levophed) was used to combat re-appearance of shock.

Temperature rose to 102.6. Pooled pharyngeal secretions required suctioning. Penicillin, dihydrostreptomycin, tetracycline and quinidine were added to therapy.

On the third day the patient took a Sippy diet. Levarterenol was stopped. Shortly before death, about 60 hours after admission, temperature was 99, blood pressure 92/50, pulse 90 and respiration 32. He became agitated, complained that no one did anything for him and refused to keep his oxygen mask on, because he felt choked by it.

Laboratory Findings:

Blood counts: 4-13-60 — Hb. 7.4 gm., Ht. 23%, WBC 18,650, Stabs. 9, Segs. 65, Lymphs. 26. **4-13-60** — Hb. 7.8 gm., Ht. 23%, WBC 17,900, Baso. 2, Stabs. 7, Segs. 85, Lymphs 6. **4-13-60** — Hb. 9.3 gms., Ht. 28%.

Coagulation time: 4-14-60 — 4′ 2″, bleeding time 3′ 8″.

Prothrombin time: 4-14-60 — 77% (Pt. 15″, C. 13″).

Chemistry: 4-13-60 — Glucose — 118 mg.%; Urea Nitrogen — 33.8 mg.%; Calcium — 4.3 mEq/L; CO-2 capacity — 22 mEq/L; Chlorides — (as NaCl) — 108 mEq/L; Potassium — 4.0 mEq/L; Sodium — 137 mEq/L; Urea Nitrogen — 18.7 mg.%; Ven der Bergh Direct — .03; Indirect — .29. **4-15-60** — CO-2 capacity — 15 mEq/L; Chlorides (as NaCl) — 108 mEq/L; Potassium — 4.1 mEq/L; Sodium — 136 mEq/L.

Serology: 4-13-60 — Negative.

Urinalysis: 4-14-60 — Amber, cloudy, acid, S.G. 1.020, Albumin negative, sugar negative, WBC 10-15/1pf, RBC 3-5, few ep. cells, 3-5/1pf hyaline casts, many bacteria.

Electrocardiogram — Left bundle branch block R in V3-4 lower than V-2.

X-rays: 4-13-60 — Portable chest: Radiographic examination of the chest reveals a moderate amount of bilateral pulmonary emphysema. There is a generalized intensification of the pulmonary vascular markings consistent with congestive failure. There is prominence of the left ventricular segment of the cardiac silhouette. The aorta is elongated, tortuous and contains calcium in its arch. There is thickening of the lobar pleura on the right. The trachea occupies its usual position.

Conclusions: Bilateral pulmonary emphysema; findings consistent with arteriosclerotic cardiovascular disease with congestive failure; thickened pleura on the right.

4-14-60 — Portable chest: Re-examination of the chest and comparision with previous study now reveals considerable edema on the entire right lung and marked amount of edema on the left. The cardiac silhouette remains unchanged. The bony thorax and diaphragm reveal no significant change.

Conclusions: Marked pulmonary edema, bilaterally.

Clinical Discussion: Dr. Wm. I. Coldwell:

This is the case of a 65 year old man admitted apparently as an emergency because of GI hemorrhage, probably in the upper GI tract, with hematemesis and melena. According to the protocol he was hypotensive and shocky, without abnormal physical findings. His pulse was 84, which is rather unusual. No mention is made of the nature of the pulse. Certainly in hemorrhage generally the rate is more rapid.

There was a history of intermittent epigastric pain which was relieved by milk, Alka Seltzer and interestingly enough, by Aspirin or Bufferin. He had had fatigue and weight loss for some time and severe pain a few days prior to admission. After vomiting of non-bloody material it was noted that the pain had decreased in intensity.

A total of six units of blood was given, presumably in the first 24 hours. It is not stated whether this patient continued to bleed and therefore required such large amounts of blood. Certainly the blood counts were compatible with blood loss, the bleeding and coagulation times were normal, the prothrombin was somewhat abnormal on admission.

The patient is stated to have become dyspneic about 36 hours after admission; he required oxygen. Even in the face of this he received more fluids, more blood, more electrolytes. Apparently congestive failure with pulmonary edema was recognized, and the patient was treated with intravenous digitalis, aminophylin, mercurial diuretics.

Rales were noted, and an enlarged, tender liver; but no edema. He was also given morphine, and tourniquets and suction were used. He apparently had quite a bit of mucus congestion. He also received antibiotics, I presume on the basis of pulmonary congestion.

Of course in bleeding in the GI track there can be a fair amount of fever, usually 100 to 100.5 from the blood absorption alone, but transfusion reaction must be considered as a cause of fever in bleeding in the GI tract. This patient was also given quinidine, for what reason I am not quite sure; he did have a tachycardia, and his EKG, which we will mention a little more in detail later, showed a rapid rate.

The patient died evidently still in congestive failure since he was no longer hypotensive, and no mention is made in the protocol that he had any further bleeding. It is stated that the medical consultant, when he first examined the patient, found no evidence of cardiac disease; and yet the initial chest film showed rather definite evidence of congestive failure. I think that we might look at these X-rays, Dr. Ravel.

X-Ray Discussion, Dr. Vincent Ravel:

The films that were taken on admission are portable examinations. They show the intensified pulmonary markings that we interpreted as consistent with congestive failure. There is some prominence of the left ventricular segment of the cardiac silhouette, the aorta is elongated and contains calcium in its arch.

On the following day there was a generalized haziness over the entire right hemithorax, the markings on the left were also increased, and

the hilar shadows showed some prominence. We concluded these changes were consistent with pulmonary edema.

Dr. Coldwell:

Along with X-ray evidence of arteriosclerotic cardiovascular disease there is an abnormal EKG. The EKG we have is one which was taken the next morning after the patient had had digitalis and had had all this treatment for failure that we mentioned. This tracing is abnormal. Deep Q-waves are present, certainly suggestive of something more than a left bundle branch block. Obviously this patient had heart disease on admission.

The significant laboratory findings here other than those already mentioned is an elevated urea nitrogen. This was no doubt due to absorption of the hemorrhage in the GI tract. There is possibly also a depression of the renal function. The association with shock could produce this renal damage at this stage of the hemorrhage.

There were some hyaline casts and some pus cells in the urine which might pre-suppose some pre-existing renal disease, probably nephrosclerosis. However, the specific gravity was quite adequate and this probably rules out any significant renal disease.

The lowering of the BUN on the second determination would be consistent with bleeding since the elevation of the BUN is usually within the first 24 hours and then begins to trail off if no further bleeding occurs. The other laboratory studies were essentially normal.

In this patient the presence of hematemesis and melena localizes the bleeding to the upper GI tract, no doubt the esophagus, stomach or duodenum. The presence of both vomiting blood and melena does not localize the site of the lesion, rather usually it is only indicative of the severity of the bleeding and the presence of a large amount of blood in the stomach.

Blood counts and hematocrits in GI hemorrhage are not of much value in very early stages. Certainly this patient had a low hematocrit and hemoglobin on admission, which would make one feel that he had bled some time prior to admission, even longer than this history states, or he had had some slow hemorrhage over a period of time prior to admission.

Certainly the presence of shock cannot be determined by the level of the blood count in the early stages. After a period of a few hours, a compensatory dilution factor occurs which will give you a more accurate interpretation of the hematocrit and hemoglobin. In the very early stages you need Evans blue blood volume determinations or similar methods to evaluate the status of the patient.

After the initial compensation of the dilution factor has occurred, you can evaluate from the hematocrit and hemoglobin how much further bleeding is occurring. Early determination of urine volume is important in indicating how much shock the patient has, since low urine output often occurs with rather profound shock. The severity of the patient's shock does not depend primarily on the amount of blood loss but on the suddeness of the blood loss.

Now for a brief review of the elementary causes of upper GI hemorrhages. Of course peptic ulcer is the most serious and common one. Bleeding usually is caused from a rupture of a small vessel at the base of the ulcer or perhaps from the gastritis surrounding the ulcer.

Occasionally a large, sclerotic blood vessel may erode, usually in the older age group. This will often cause a fatal hemorrhage. In this case a rather scanty history elicited symptoms which would be consistent with a peptic ulcer. This patient had a decrease in his pain prior to admission, which would make one suspect a peptic ulcer. We see that rather frequently, that the pain will be relieved when an ulcer bleeds.

The second big cause of hemorrhage is gastritis or esophagitis, and certainly in ulcers bleeding may occur from a site even remote from the ulcer, such as an area of gastritis. This patient admitted to a moderate intake of alcohol, but this history often is unreliable. Many times a patient will claim moderate use of alcohol and this is the same as the usual two beers. This patient had also taken some Aspirin and Bufferin which of course can produce hyperacidity, gastritis; and has been reported to cause bleeding. Certainly the amount of antiacid in Bufferin is not sufficient to counteract hyperacidity, notwithstanding the TV commercials.

There is a higher incidence of peptic ulcer in pulmonary emphysema, and it would appear from this report that this patient had a fair degree of emphysema.

Carcinoma of the stomach comprises about three per cent of the cases of hemorrhage. Certainly this massive hemorrhage is not the usual picture that one sees. It can occur, but generally the bleeding is slower. This patient did complain of variable appetite and weight loss. He is in the age group for cancer, so certainly one must consider a cancer or malignant ulcer in this case.

Portal hypertension: About 10 per cent of the cases of bleeding fall into this group. This patient had no physical evidence of cirrhosis. He did have two liver function tests, a cephalin flocculation which was 1+ at 48 hours, and a thymol turbidity which was two units, both within normal range.

I think that as a single screening test for cirrhosis a 45 minute BSP test is probably the best test. However, in rather advanced cirrhosis the test may be very close to normal. Of course in cirrhosis the incidence of peptic ulcer is much higher than in other individuals, and the bleeding may often occur from the ulcer rather than from esophageal varices.

One must consider the other more rare causes of hemorrhage, such as benign tumors of the stomach, upper intestinal tract, hiatus hernia, various blood dyscrasias, or hereditary hemorrhagic telangiectasis. This patient had no diagnostic studies or laparotomy, so one would really be stabbing in the dark to make such a surmise.

It appears to me that this patient was definitely over-transfused. For an elderly individual with apparent damaged myocardium he was given a tremendous amount of blood. It was noted that the day when his blood was still being given the hematocrit had risen to around 40 per cent, hematocrit was 45, hemoglobin was 13.5; and I see little need to over-transfuse these individuals unless they continue to bleed, and then one should certainly consider laparotomy if they are at all in any type of condition for surgery. Certainly in an already damaged heart the tremendous overload of return to the right heart could throw this patient into congestive failure. It appears to me that he definitely developed congestive failure in this manner.

Of course it is possible that the patient during his period of hypotension had a myocardial infarction, which is not uncommon in shock from any cause. As we mentioned before, the EKG is rather suggestive to me of some recent myocardial damage. Of course it is well known that the diagnosis of acute recent myocardial infarction in the presence of a left bundle branch block is a rather difficult thing to do by electrocardiography. It appears that this patient was over-transfused and that he was precipitated at least into congestive heart failure by too much blood.

Therefore, my diagnoses are: **1.** Upper GI hemorrhage, secondary to bleeding peptic ulcer, possibly malignant; **2.** Congestive heart failure precipitated by excessive intravenous fluid; **3.** Arteriosclerotic heart disease, left bundle branch block and possible recent myocardial infarction.

Dr. Russell Deter:

GI bleeding is always a fearsome thing. The surgical mortality amongst the dying is always high. If a patient on admission has a blood pressure of 70/40 and a pulse of 84, blood pressure and a pulse taken every 10 to 30 minutes for several hours will establish quickly whether the patient is still bleeding or not, and this has to be determined as soon as possible.

I do not think that a pulse of 84 is consistent with continued bleeding, if it is constant. I agree with Dr. Coldwell that six units of blood would be too much even if he is bleeding. If he required that much, he should have been operated on. These patients sometimes die on the table; but they die off the table, too. I would like to know the times in relation between the blood counts on the day of admission and the transfusions.

I believe in GI bleeding that blood should be given most judiciously, that it should be given extremely slowly, and with particular caution not to elevate the blood pressure. Often a clot will form at the end of a bleeding vessel and by giving the patient a lot of blood, one will sometimes raise the pressure sufficiently to knock out the clot and re-start the bleeding.

I would mention that we surgeons would prefer to have the bleeding stopped, to establish the location of the bleeding point, and then operate. This is not always feasible. I would certainly like to put in a word of caution about transfusions. Transfusions are live-saving procedures, but they are life-terminating ones, too.

Dr. Jack Postlewaite:

I think this patient had an ulcer and I think we should discuss the question of therapy. Granted that the patient had an ulcer, there is valid criticism why there was no surgical intervention, specially if radiology could have disclosed the location of the ulcer and whether it was benign or malignant. It is granted that hemoglobin and hematocrit should be taken regularly and that they are very important. Also the staff must observe whether the colon is filled with blood and how much blood is lost through the rectum.

I think replacing blood by knowing what was lost is important. The replacement is specially important in a cardiac patient who is anemic because of anoxia due to anemia; will not be tolerated by a damaged myocardium. The only other comment regarding transfusions is the possibility of a transfusion reaction. This may occur early or late and must be guarded against.

A final remark in differential diagnosis: severe hemorrhage can occur from gastritis, specially in the alcoholic. These people bleed actively and vividly like peptic ulcers and present a grave problem to the surgeon. As far as the cardiac status of the patient is concerned, I don't think it represents a contra-indication to surgery.

Clinical Diagnosis: Gastric ulcer.

Dr. Coldwell's Diagnoses: 1. Upper GI hemorrhage, secondary to bleeding peptic ulcer, possibly malignant; **2.** Congestive heart failure precipitated by excessive intravenous fluid; **3.** Arteriosclerotic heart disease, left bundle branch block and possible recent myocardial infarction.

Pathological Diagnoses: 1. Extremely severe coronary sclerosis with fresh subintimal hemorrhage in the right coronary artery; **2.** Extensive recent infarction of myocardium on the posterior wall of left ventricle and interventricular septum; **3.** Extensive myocardial scarring; **4.** Acute pulmonary edema; **5.** Acute and chronic passive hyperemia of the liver; **6.** Bleeding peptic ulcer of duodenum.

Pathological Discussion: Dr. Bornstein:

We can then come to the autopsy protocol. For Dr. Van Wagoner's benefit, he might be a little bit suspicious, being new with us, we really are on the honor system, in spite of what I am going to say now. Dr. Coldwell hadn't the slightest chance or opportunity to look at the autopsy protocol.

On autopsy there was an elderly, fairly well nourished man, who didn't look too pale. There was some pleural effusion; there was minimal ascites. The large intestine was filled with clotted blood, the small intestine was empty, indicating to me that at the time of death the active phase of bleeding of the ulcer had subsided.

The ulcer itself was located directly beneath the pylorus in the first part of the duodenum on the posterior wall, a typical punched out peptic ulcer which measured 1.5 cm. in diameter and rested on the pancreas without penetrating it. There were a few petechial hemorrhages on the pericardium. The entire myocardium, specially in the region of the apex and septum, was markedly thinned out and there were large areas on the posterior wall and septum where the myocardium had been replaced by grayish-white scar tissue.

In addition there was an area measuring about 3 cm. in the posterior wall of the left ventricle where there was total loss of the myocardial pattern and there was yellowish, soft, homogeneous tissue. The left main descending branch showed extensive old calcification, as did the left main circumflex branch. The right coronary ostium was narrow and there was an area of constriction two cm. below the right coronary ostium where there was a fresh subintimal hemorrhage.

Microscopically the section from the stomach shows a typical benign peptic ulcer with a partially eroded artery. There was a thrombus at the end of the artery which may have caused termination of the hemorrhage. Sections from the myocardium showed scarring and areas of necrosis with extreme infiltration of segmented granulocytes and beginning necrosis, indicating an infarct of about three days duration. We then have in this patient, as predicted by Dr. Coldwell, two lesions: a peptic ulcer, bleeding; and rather severe coronary heart disease which finally produced infarction, scarring, decompensation and death.

In view of the various questions of hypo-oxemia of the myocardium on the one hand and overloading the myocardium with fluids on the other,

it would be nice to establish a definite correlation here. The patient was transfused immediately upon admission and died three days later. If you get a real yellow infarct, with complete disappearance of red blood cells from the infarction and nearly exclusive infiltration by segmented granulocytes, you have an infarct that is at least 48 hours old, but not much older than 48 hours.

I think we can say with reasonable certainty that the infarction occurred after and not before admission. Whether it then was still due to the existing anoxemia, or to the overloading, it is extremely difficult to say. It occurs to me that if you have extremely narrow and poorly functioning coronaries in a rather anemic patient, blood viscosity is much lower and should permit easier permeability of the coronaries by whatever red blood cells are available. If you increase the viscosity considerably, the impediment to the blood flow through a coronary system may have become much larger and thus contribute to the development of an infarct.

Dr. Deter:

I would like to answer in part the question of operating on a patient with a bleeding ulcer who has a badly damaged heart. To save this patient's life it isn't necessary to remove the stomach, which is a more or less formidable procedure in the presence of heart disease. If the patient continues to bleed, for the information of the house staff, a very simple maneuver can be done that only takes a few minutes.

You establish of course that the bleeding is coming from an ulcer, it may be gastric or duodenal. If it's duodenal you split the pylorus longitudinally, take a 20 cotton suture, take a figure eight stitch through the bed of the ulcer where the bleeding is from, be it pyloric or gastric, close the pylorus as you do in a pyloroplasty, get out and turn him back to the internist. You have stopped the bleeding, it is his worry now.

Dr. James C. Kussy:

All the anesthetic agents are myocardial depressants and I think that to give a patient anesthesia, a patient with a coronary, is really asking for it. On the other hand, it is worth the risk if it is a matter of stopping a hemorrhage that is also a life or death matter.

In regard to anesthesia for patients in heart failure, I have never given an anesthetic to a patient in heart failure, I don't know what the experience of the other anesthetists is. I think that I personally would use cyclopropane which would be giving the patient about 80 per cent oxygen all during that time, and it is an agent which tends to support blood pressure. I think it might work well in such a situation.

Coming Meetings

Southwest Obstetrical and Gynecological Society, Annual Meeting, Riviera Hotel, Las Vegas, Nev., Nov. 7-8, 1960.

Medical Society of the United States and Mexico, Annual Meeting, Guadalajara, Nov. 8-10, and Mazatlan, Nov. 11-12, 1960.

American College of Surgeons, Arizona Chapter, Fall Clinical Congress, Tidelands Motel, Tucson, Nov. 17-19, 1960.

American Rheumatism Association, Seventh Interim Scientific Session, Sheraton-Dallas Hotel, Dallas, Dec. 9-10, 1960.

American Cancer Society, Arizona Division, Ninth Annual Cancer Seminar, Tidelands Motor Inn, Tucson, Jan. 12-14, 1961.

Arizona Heart Association, Fourth Annual Cardiac Symposium, Biltmore Hotel, Phoenix, Jan. 27-28, 1961.

Texas Orthopaedic Association, Galveston, Texas, April 24, 1961.